● PRINTER RUSH ●

(PTO ASSISTANCE)

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[RUSH] **MESSAGE:** Specification: page 11 line # 19 - U.S. patent Application No ____, filed on ____ is missing. please provide.

Thank you.

[XRUSH] **RESPONSE:**

INITIALS:

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REV 10/04

Certain therapeutic drugs contain primary amines and are among the preferred agents. These include the anthracycline family of drugs, the vinca drugs, the mitomycins, the bleomycins, the cytotoxic nucleosides, the pteridine family of drugs, diynenes, the podophyllotoxins, and the taxanes. Particulary useful members of these classes include, for example, doxorubicin, daunorubicin, carminomycin, idarubicin, epirubicin, aminopterin, methotrexate, methopterin, mitomycin C porfiromycin, 5-flurouracil, cytosine arabinoside, etoposide, melphalan, vincristine, vinblastine, vindesine, 6-mercaptopurine, and the like.

Other therapeutic drugs are required to have primary amines introduced by chemical or biochemical synthesis, for example sesquiterpene-lactones such as thapsigargin, and thapsigargicin and many others know to those skilled in the art. The thapsigargins are a group of natural products isolated from species of the umbelliferous genus *Thapsia*. The term thapsigargins has been defined by Christensen, *et al.*, *Prog. Chem. Nat. Prod.*, 71 (1997) 130-165. These derivatives contain a means of linking the therapeutic drug to carrier moieties, including peptides and antibodies. The peptides and antibodies can include those which specifically interact with antigens including hK2. The interactions can involve cleavage of the peptide to release the therapeutic analogs of sesquiterpene-γ-lactones. Particular therapeutic analogs of sesquiterpene-γ-lactones, such as thapsigargins, are disclosed in United States Patent Application No. 09/588,822, filed June 7, 2000, entitled "Tissue Specific Prodrug," and United States Patent Application No. 09/588921 ___, filed June 7, 2000 ~~on even date herewith~~, entitled "Tissue Specific Prodrug," both of which are incorporated herein in their entireties.

For example, thapsigargins with alkanoyl, alkenoyl, and arenoyl groups at carbon 8 or carbon 2, can be employed in the practice of the invention disclosed herein. Groups such as CO-$(CH=CH)_{n1}$-$(CH_2)_{n2}$-Ar-NH_2, CO-$(CH_2)_{n2}$-$(CH=CH)_{n1}$-Ar-NH_2, CO-$(CH_2)_{n2}$-$(CH=CH)_{n1}$-CO-NH-Ar-NH_2 and CO-$(CH=CH)_{n1}$-$(CH_2)_{n2}$-CO-NH-Ar-NH_2 and substituted variations thereof can be used as carbon 8 substituents, where n1 and n2 are from 0 to 5, and Ar is any substituted or unsubstituted aryl group. Substituents which may be present on Ar include short and medium chain alkyl, alkanoxy, aryl, aryloxy, and alkenoxy groups, nitro, halo, and primary secondary or tertiary amino groups, as well as such groups connected to Ar by ester or amide linkages. In other embodiments of thapsigargin analogs, these substituent groups are represented by unsubstituted, or alkyl-, aryl-, halo-, alkoxy-, alkenyl-, amido-, or amino-substituted CO-$(CH_2)_{n3}$-